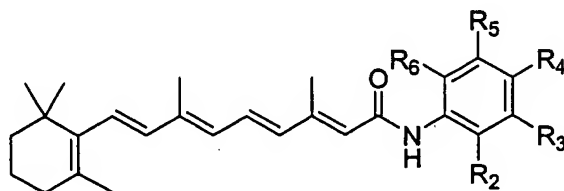


## CLAIMS

What is claimed is:

1. A method of preparing an arylretinamide comprising:
  - a) reacting hexachloroacetone with a solvent-suspended resin-bound triphenylphosphine to provide a suspension comprising an activated chlorinating reagent;
  - b) reacting retinoic acid with the activated chlorinating reagent to provide retinoyl chloride;
  - c) adding pyridine and a select arylamine to the reaction mixture and stirring the resulting mixture for a time and at a temperature sufficient for the arylamine to react with the retinoyl chloride and provide the arylretinamide.
2. The method of claim 1 further comprising the step of purifying the arylretinamide from the suspension.
3. The method of claim 2 wherein purification is accomplished by treatment of the reaction mixture with solid phase reagents to remove unreacted starting materials followed by chromatography.
4. The method of claim 1 wherein step (a) is performed at a temperature ranging from about 0°C to room temperature.
5. An arylretinamide for inducing apoptosis in a cancer cell, said arylretinamide having Structure A, B, or C below:



**Structure A**

wherein

$R_2$  is H, OH,  $\text{NO}_2$ ,  $\text{CH}_2\text{OH}$ , a halide, or an alkyl comprising 1-4 carbon atoms,

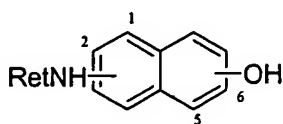
$R_3$  is H, OH,  $\text{NO}_2$ ,  $\text{CO}_2\text{CH}_3$ ,  $\text{CO}_2\text{CH}_2\text{CH}_3$ ,  $\text{CO}_2(\text{CH}_2)_2\text{CH}_3$ ,  $\text{CO}_2(\text{CH}_2)_3\text{CH}_3$ ,  $\text{CO}_2\text{H}$ ,  $\text{CH}_2\text{OH}$ , a halide, or an alkyl comprising 1-4 carbon atoms;

$R_4$  is H, OH,  $\text{OCH}_3$ ,  $\text{OCH}_2\text{CH}_3$ ,  $\text{O}(\text{CH}_2)_2\text{CH}_3$ ,  $\text{O}(\text{CH}_2)_3\text{CH}_3$ ,  $\text{SO}_2\text{CH}_3$ ,  $\text{SO}_2\text{CH}_2\text{CH}_3$ ,  $\text{SO}_2(\text{CH}_2)_2\text{CH}_3$ ,  $\text{SO}_2(\text{CH}_2)_3\text{CH}_3$ ,  $\text{NH}_2$ ,  $\text{NHCOCH}_3$ ,  $\text{NHCOCH}_2\text{CH}_3$ ,  $\text{NHCO}(\text{CH}_2)_2\text{CH}_3$ ,  $\text{NHCO}(\text{CH}_2)_3\text{CH}_3$ ,  $\text{NHCOCF}_3$ ,  $\text{N}_3$ ,  $\text{NCS}$ , a halide, an alkyl comprising 1-4 carbon atoms, or  $\text{NHCOCH}_2\text{X}$ , wherein X is a halide;

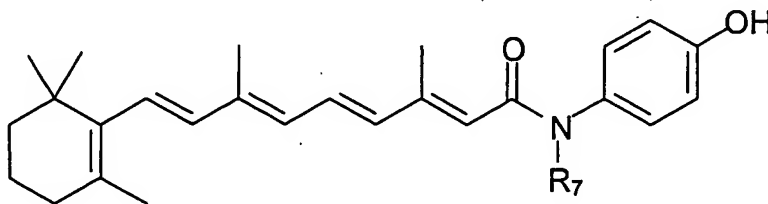
$R_5$  is H,  $\text{NO}_2$ ,  $\text{C}(\text{CH}_3)_3$ ,  $\text{C}(\text{CH}_2\text{CH}_3)_3$ ,  $\text{C}((\text{CH}_2)_2\text{CH}_3)_3$ ,  $\text{C}((\text{CH}_2)_3\text{CH}_3)_3$ ,  $\text{CO}_2\text{CH}_3$ ,  $\text{CO}_2\text{CH}_2\text{CH}_3$ ,  $\text{CO}_2(\text{CH}_2)_2\text{CH}_3$ ,  $\text{CO}_2(\text{CH}_2)_3\text{CH}_3$ , a halide, or an alkyl comprising 1-4 carbon atoms, and

$R_6$  is H,  $\text{CO}_2\text{H}$ ,  $\text{CO}_2\text{CH}_3$ ,  $\text{CO}_2\text{CH}_2\text{CH}_3$ ,  $\text{CO}_2(\text{CH}_2)_2\text{CH}_3$ ,  $\text{CO}_2(\text{CH}_2)_3\text{CH}_3$ , a halide or an alkyl comprising 1-4 carbon atoms;

provided however that when  $R_2$ ,  $R_3$ ,  $R_4$ ,  $R_5$ , and  $R_6$  are all H,  $R_4$  is not OH or  $\text{OCH}_2\text{CH}_3$ ; and also provided that when  $R_3$ ,  $R_5$ , and  $R_6$  are all H, and  $R_2$  is OH,  $R_4$  is not  $\text{CO}_2\text{CH}_3$ .

**Structure B**

wherein the OH group is at position 2,4, or 5 when the retinamido group is at linked to position 1, and the OH group is at position 3 when the retinamido group is linked to position 2.

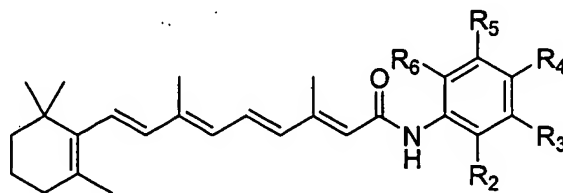


**Structure C**

wherein R<sub>7</sub> is C<sub>1</sub> to C<sub>4</sub> alkyl.

6. The arylretinamide of claim 5 wherein the arylretinamide is a halohydroxyphenyl retinamides which comprises a phenyl moiety that is optionally substituted with an alkyl group .
7. The arylretinamide of claim 6 wherein the phenyl moiety is substituted with a methyl group.
8. The arylretinamide of claim 6 wherein the halo group is an iodo group.
9. The arylretinamide of claim 5 wherein the arylretinamide is a hydroxy-alkylphenyl retinamides or hydroxy-alkoxyphenyl retinamide, wherein the alkyl groups attached to the phenyl moiety comprise from 1 to 4 carbon atoms.
10. The arylretinamide of claim 9 wherein the arylretinamide is a hydroxy-methylphenyl or hydroxy-methoxyphenyl retinamide.
11. The arylretinamide of claim 5 is a hydroxy-nitrophenyl retinamides or alkylsulfonyl-hydroxy retinamides.
12. The arylretinamide of claim 11 wherein the arylretinamide is an ethylsulfonyl-hydroxy, retinamides.
13. The arylretinamide of claim 5 wherein the arylretinamide is a hydroxy-naphthylphenyl retinamide.

14. The arylretinamide of claim 5 wherein the arylretinamide is an N-alkyl(hydroxyphenyl)retinamides.
15. The arylretinamide of claim 5 wherein the arylretinamide is an aminophenyl retinamides.
16. The arylretinamide of claim 5 wherein the arylretinamide is an alkylhydroxyphenyl retinamides.
17. The arylretinamide of claim 5 wherein the arylretinamide is a carboxy-hydroxyphenyl retinamides selected from the group consisting of *N*-(2'-hydroxy-3'-carboxymethylphenyl)retinamide, *N*-(2'-hydroxy-3'-carboxyphenyl)retinamide, *N*-(2'-hydroxy-6'-carboxymethylphenyl)retinamide, *N*-(2'-hydroxy-6'-carboxyphenyl)retinamide, *N*-(3'-hydroxy-4'-carboxymethylphenyl)retinamide, *N*-(3'-hydroxy-4'-carboxyphenyl)retinamide, *N*-(2'-hydroxy-5'-carboxymethylphenyl)retinamide, *N*-(2'-hydroxy-4'-carboxyphenyl)retinamide, *N*-(4'-hydroxy-3'-carboxymethylphenyl)retinamide, and *N*-(4'-hydroxy-3'-carboxyphenyl)retinamide.
18. An arylretinamide having Structure A below



Structure A

wherein

$R_2$  is H, OH,  $\text{NO}_2$ ,  $\text{CH}_2\text{OH}$ , a halide, or an alkyl comprising 1-4 carbon atoms,

R<sub>3</sub> is H, OH, NO<sub>2</sub>, CO<sub>2</sub>CH<sub>3</sub>, CO<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>, CO<sub>2</sub>(CH<sub>2</sub>)<sub>2</sub>CH<sub>3</sub>, CO<sub>2</sub>(CH<sub>2</sub>)<sub>3</sub>CH<sub>3</sub>, CO<sub>2</sub>H, CH<sub>2</sub>OH, a halide, or an alkyl comprising 1-4 carbon atoms;

R<sub>4</sub> is H, OH, OCH<sub>3</sub>, OCH<sub>2</sub>CH<sub>3</sub>, O(CH<sub>2</sub>)<sub>2</sub>CH<sub>3</sub>, O(CH<sub>2</sub>)<sub>3</sub>CH<sub>3</sub>, SO<sub>2</sub>CH<sub>3</sub>, SO<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>, SO<sub>2</sub>(CH<sub>2</sub>)<sub>2</sub>CH<sub>3</sub>, SO<sub>2</sub>(CH<sub>2</sub>)<sub>3</sub>CH<sub>3</sub>, NH<sub>2</sub>, NHCOCH<sub>3</sub>, NHCOCH<sub>2</sub>CH<sub>3</sub>, NHCO(CH<sub>2</sub>)<sub>2</sub>CH<sub>3</sub>, NHCO(CH<sub>2</sub>)<sub>3</sub>CH<sub>3</sub>, NHCOCF<sub>3</sub>, N<sub>3</sub>, NCS, a halide, an alkyl comprising 1-4 carbon atoms, or NHCOCH<sub>2</sub>X, wherein X is a halide;

R<sub>5</sub> is H, NO<sub>2</sub>, C(CH<sub>3</sub>)<sub>3</sub>, C(CH<sub>2</sub>CH<sub>3</sub>)<sub>3</sub>, C((CH<sub>2</sub>)<sub>2</sub>CH<sub>3</sub>)<sub>3</sub>, C((CH<sub>2</sub>)<sub>3</sub>CH<sub>3</sub>)<sub>3</sub>, CO<sub>2</sub>CH<sub>3</sub>, CO<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>, CO<sub>2</sub>(CH<sub>2</sub>)<sub>2</sub>CH<sub>3</sub>, CO<sub>2</sub>(CH<sub>2</sub>)<sub>3</sub>CH<sub>3</sub>, a halide, or an alkyl comprising 1-4 carbon atoms, and

R<sub>6</sub> is H, CO<sub>2</sub>H, CO<sub>2</sub>CH<sub>3</sub>, CO<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>, CO<sub>2</sub>(CH<sub>2</sub>)<sub>2</sub>CH<sub>3</sub>, CO<sub>2</sub>(CH<sub>2</sub>)<sub>3</sub>CH<sub>3</sub>, a halide, or an alkyl comprising 1-4 carbon atoms;

provided that when R<sub>2</sub>, R<sub>3</sub>, R<sub>4</sub>, R<sub>5</sub>, and R<sub>6</sub> are all H, R<sub>4</sub> is not OH, OCH<sub>3</sub>, OCH<sub>2</sub>CH<sub>3</sub>, or O(CH<sub>2</sub>)<sub>2</sub>CH<sub>3</sub>; and also

provided that when R<sub>3</sub>, R<sub>5</sub>, and R<sub>6</sub> are all H, and R<sub>2</sub> is OH, R<sub>4</sub> is not CO<sub>2</sub>CH<sub>3</sub> or CO<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>.

19. A method of inducing apoptosis in a cancer cell comprising contacting the cancer cell with an arylretinamide of claim 1.

20. A method of treating cancer in a subject in need of said treatment, comprising administering one or more arylretinamides of claim 1 to the subject.

21. The method of claim 20 wherein said method further comprises administering calcium glucarate to the subject.